

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Chico Gholz on October 2, 2008.

The application has been amended as follows:

Please cancel withdrawn claims 38-53.

Please amend claim 28 as follows:

Claim 28: A method for controlling ~~sealing~~ the formation of a seal between of a biological element comprising a membrane on and the edges of a through-opening made in a support, wherein in which the biological element is labeled with a tracer that emits a light radiation, the support comprises a layer of a material configured to trap the light radiation by internal reflection, and ~~the edges of the through-opening on which the biological element is sealed are~~ is located in the layer, the method comprising:

- a) ~~sealing~~ forming the seal between the biological element ~~on~~ and the edges of the through-opening by creating a low pressure in the through-opening to cause the biological element to partially penetrate the opening;
- b) measuring intensity of light radiation ~~trapped~~ internally reflected in the layer at predetermined distances from the through-hole; and

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c) ~~controlling sealing of the biological element by~~ comparing the intensity thus measured with at least one reference value to determine when the seal is obtained;

wherein a) and b) can be carried out successively or simultaneously.

Claim 30: A method according to Claim 29, in which the fluorescent tracer is one of:

- a) an organic fluorophore chemically coupled to one or more membrane proteins of the biological element,
- b) an antibody labeled with an organic fluorophore, which is directed against a membrane protein of the biological element and which is attached to the biological element by an antigen-antibody reaction, ~~or~~ and
- c) a fluorescent membrane protein which is expressed by the biological element.

Claim 31: A method according to Claim 28, in which the layer of material capable of trapping the light radiation is made of one of the following:

- a) organic or mineral glass,
- b) silica,
- c) silicon nitride,
- d) titanium dioxide,
- e) hafnium dioxide,
- f) alumina,
- g) silica loaded with potassium or silver ions, and ~~or~~
- h) a synthetic polymer.

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Claim 32: A method according to Claim 28, further comprising, prior to a) or between a) and b), providing the support with a means for extracting light radiation trapped in the layer of material capable of trapping the light radiation.

Claim 33: A method according to Claim 32, further comprising, prior to a) or between a) and b), placing, ~~opposite the layer of material capable of trapping the light radiation,~~ a means for collecting the light radiation extracted from the layer over the layer of material capable of trapping the light radiation.

Claim 36: A method according to Claim ~~28~~ 35, in which a) and b) are carried out simultaneously.

Claim 54: A method for ~~controlling establishment of~~ establishing a high-resistance seal between ~~one~~ a biological element comprising a membrane and the edges of a through-opening ~~made~~ in a support by a patch-clamp technique, in which the biological element is labeled with a tracer that emits a light radiation, wherein the support comprises a layer of material configured to trap the light radiation by internal reflection, and the ~~edges of the through-opening on which the biological element is sealed are~~ is located in the layer, the method comprising:

- a) ~~sealing~~ forming the seal between the biological element ~~on~~ and the edges of the through-opening by creating a low pressure in the through-opening to cause the biological element to partially penetrate the opening;
- b) measuring intensity of light radiation trapped in the layer; and

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c) ~~controlling sealing of the biological element by~~ comparing the intensity ~~thus~~ measured with at least one reference value to determine when the high-resistance seal is established;

wherein a) and b) can be carried out successively or simultaneously.

### ***Reasons for Allowance***

The following is an examiner's statement of reasons for allowance: The prior art fails to teach a method wherein the measurement of light from a labeled biological element that is internally reflected in a layer of light-trapping material in order to determine when a seal is formed between the biological element and the edges of a through hole. Furthermore, there is no motivation to do so, as this would require not only a label on the biological element capable of emitting light radiation, but it would also require the hole to be at least partially formed in a layer of light trapping material for the seal to be formed, and it would also require optical detectors to measure the light internally reflected within the light trapping material.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/  
Patent Examiner, Art Unit 1641